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Substitute for form 1449B/PTO

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Date Submitted: July 10, 2002

(use as many sheets as necessary)

Sheet 1 of 6

## Complete if Known

Application Number	09/986,119
Filing Date	11/07/2001
First Named Inventor	David M. Goldenberg
Group Art Unit	1645
Examiner Name	Unassigned
Attorney Docket Number	018733-1058

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Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	Number	Kind Code <sup>2</sup> (if known)			
1	5,995,073		Rybak, Youle, Newton, and Nichols	09-21-1999	
2	5,840,840		Rybak, Youle, Newton, and Nichols	11-24-1998	
3	4,816,567		Cabilly, et al.	03-28-1989	
4	5,559,212		Wojciech J. Ardelt	09-24-1996	
5	5,728,805		Wojciech J. Ardelt	03-17-1998	

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	6	EP	0 173 494	A2		07-08-1985	Previously cited in Parent Application as all that follows	
	7	WO	87/02671			10-27-1986		
	8	WO	88/09344	A		05-19-1988		
	9	WO	97/02588			06-20-1996		
	10	PCT	US98/05453			03-19-1998		

## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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	11	Rybak, et al. <i>PNAS</i> , 89:3165-3169, 1992	
	12	De Prisco, et al., " <i>A Ribonuclease from human seminal plasma active on double-stranded RNA</i> ", <i>Biochim, Biophys. Acta</i> 788:356-363 (1984)	
	13	Jones, et al., " <i>Replacing the complementarity-determining regions in a human antibody with those from a mouse</i> ", <i>Nature</i> 321: 522-525 (5/29/86)	
	14	Williams, et al., " <i>Production of antibody-tagged enzymes by myeloma cells: application to DNA polymerase I Klenow fragment</i> ", <i>Gene</i> 43:319-324 (1986)	
	15	St. Clair, et al., " <i>Angiogenin abolishes cell-free protein synthesis by specific ribonucleolytic inactivation of ribosomes</i> ", <i>Proc. Natl. Acad. Sci. USA</i> 84:8330-8334 (12/87)	
	16	Riechmann, et al., " <i>Reshaping human antibodies for therapy</i> ", <i>Nature</i> 332: 323-327 (3/24/1988)	

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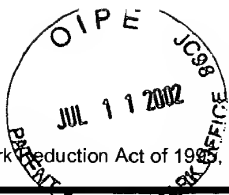
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Substitute Form 1449B/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		<b>Application Number</b>	09/986,119
Date Submitted: July 10, 2002		<b>Filing Date</b>	11/07/2001
(use as many sheets as necessary)		<b>First Named Inventor</b>	David M. Goldenberg
		<b>Group Art Unit</b>	1645
		<b>Examiner Name</b>	Unassigned
<b>Sheet</b>	2 of 6	<b>Attorney Docket Number</b>	018733-1058

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h	17	Huston, et al., "Protein engineering of antibody binding sites: Recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in Escherichia coli", Proc. Natl. Acad. Sci., USA 85:5878-5883 (8/1988)	
	18	Bird, et al., "Single-chain antigen-binding proteins", Science 242:423-426 (10/21/1998)	
	19	Darzynkiewicz, et al., "Cytostatic and cytotoxic effects of Pannon (P-30 Protein), a novel anticancer agent", Cell Tissue Kinet. 21:169-182 (1988)	
	20	Khazaeli, et al., "Immunology", Proceedings of AACR 29:418 (1988)	
	21	Nishimura, et al., "Expression and function of a CD 5 cDNA in human and murine T cells", Eur. J. Immunol. 18:747-753 (1988)	
	22	Griffin, et al., "Immunotoxin therapy: Assessment by animal models", Immunotoxins, Boston/Dordrecht/Lancaster, Kluwer Academic Publishers, p. 433-455 (1988)	
	23	Chaudhary, et al., "A recombinant immunotoxin consisting of two antibody variable domains fused to Pseudomonas exotoxin", Nature 339: 394-397 (6/1/1989)	
	24	Ward, et al., "Binding activities of a repertoire of single immunoglobulin variable domains secreted from Escherichia coli", Nature 341:544-546 (10/12/1989)	
	25	Batra, et al., "Antitumor activity in mice of an immunotoxin made with antitransferrin receptor and a recombinant form of Pseudomonas exotoxin", Proc. Natl. Acad. Sci. USA 86:8545-8549 (11/89)	
	26	Mikulski, et al., "Striking increase of survival of mice bearing M109 madison carcinoma treated with a novel protein from amphibian embryos", J. Nat'l. Cancer Inst. 82(2):151-153 (1/17/1990)	
	27	Chaudhary, et al., "A rapid method of cloning functional variable-region antibody genes in Escherichia coli as single-chain immunotoxins", Proc. Natl. Acad. Sci. USA 87:1066-1070 (2/1990)	
	28	Casadei, et al., "Expression and secretion of aequorin as a chimeric antibody by means of a mammalian expression vector", Proc. Natl. Acad. Sci. USA 87:2047-2051 (3/1990)	

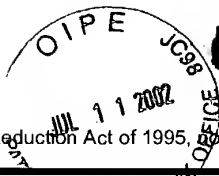
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First Named Inventor	David M. Goldenberg				
Group Art Unit	1645				
Examiner Name	Unassigned				
Attorney Docket Number	018733-1058				
Sheet	3	of	6		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
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hsp	29	Goodson, et al., "Site-directed pegylation of recombinant interleukin-2 at its glycosylation site", Bio-Technology 8:343-346 (4/1990)	
	30	Batra, et al., "Anti-tac (Fv)-PE40, a single chain antibody Pseudomonas fusion protein directed at interleukin 2 receptor bearing cells", J. Biol. Chem. 265:15198-15202 (9/5/1990)	
	31	Mikulski, et al., "Tamoxifen and trifluoroperazine (Stelazine) potentiate cytostatic/cytotoxic effects of P-30 protein, a novel protein possessing anti-tumour activity", Cell Tissue Kinet. 23:237-246 (1990)	
	32	Winter, et al., "Man-made antibodies", Nature 349:293-299 (1/24/1991)	
	33	Rybak, et al., "Human Cancer Immunology II. Clinical use of immunotoxins. Monoclonal antibodies conjugated to protein toxins", Immunology and Allergy Clinics of North America 11(2):359-380, W.B. Saunders Co. (5/1991)	
	34	Pearson, J.W., et al., "Reversal of Drug Resistance in a Human Colon Cancer Xenograft Expressing MDR1 Complementary DNA by in vivo administration of MRK-16 monoclonal Antibody", J. Natl. Cancer Inst. 83(19):1386-1391 (10/2/1991)	
	35	Ghetie, et al., "Antitumor activity of Fab' and IgG-anti-CD22 immunotoxins in disseminated Human B lymphoma grown in mice with severe combined immunodeficiency disease: effect on tumor cells in extranodal sites", Cancer Res. 51:5876-5880 (11/1/1991)	
	36	Hoogenboom, et al., "Construction and expression of antibody-tumor necrosis factor fusion proteins", Molecular Immunology 28 (9):1027-1037 (11/4/1991)	
	37	Rybak, et al., "Cytotoxic potential of ribonuclease and ribonuclease hybrid proteins", J. Biol. Chem. 266:21202-21207 (11/5/1991)	

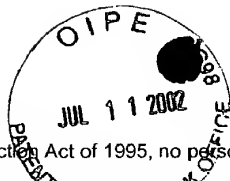
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: July 10, 2002

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Sheet 4 of 6

**Complete if Known**

Application Number	09/986,119
Filing Date	11/07/2001
First Named Inventor	David M. Goldenberg
Group Art Unit	1645
Examiner Name	Unassigned

Attorney Docket Number 018733-1058

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**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

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h g	38	Hoogenboom, et al., " <b>Targeting of tumor necrosis factor to tumor cells: secretion by myeloma cells of a genetically engineered antibody-tumor necrosis factor hybrid molecule</b> ", Biochem. Biophys. Acta 1096:345-354 (11/20/1991)	
	39	Ardelt, et al., " <b>Amino acid sequence of an anti-tumor protein from Rana pipiens oocytes and early embryos</b> ", J. Biol. Chem. 266(1):245-251 (1991)	
	40	Uckun, et al., " <b>In vivo efficacy of B43 (anti-CD19) -pokeweed antiviral protein immunotoxin against human Pre-B cell acute lymphoblastic leukemia in mice with severe combined immunodeficiency</b> ", Blood 79 (9):2201-2214 (5/1/1992)	
	41	Newton et al., " <b>Cytotoxic ribonuclease chimeras</b> ", J. Biol. Chem. 267 (27):19572-19578 (9/25/1992)	
	42	Grossbard, et al., " <b>Anti-B4 blocked ricin: A phase I trial of 7-day continuous infusion in patients with B-cell neoplasms</b> ", J. Clin. Oncol. 11(4):726-737	
	43	Grossbard, et al., " <b>Adjuvant immunotoxin therapy with anti-B4-blocked ricin after autologous bone marrow transplantation for patients with B-cell non-Hodgkin's lymphoma</b> ", Blood 81(9):2263-2271 (5/1/93)	
	44	Amlot, et al., " <b>A Phase I study of an anti-CD22-deglycosylated ricin A chain immunotoxin in the treatment of B-cell lymphomas resistant to conventional therapy</b> ", Blood 82(9):2624-2633 (11/1/93)	
	45	Rybak, et al., " <b>Cytotoxic onconase and ribonuclease A chimeras: Comparison and in Vitro characterization</b> ", Drug Delivery 1:3-10 (1993)	
	46	Newton, et al., " <b>Toxicity of an antitumor ribonuclease to Purkinje neurons</b> ", J. Neurosci. 14(2):538-544 (2/94)	

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Sheet 5 of 6

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LH	47	Rybak, et al., " <i>RNase and RNase immunofusions for cancer therapy</i> ", Tumor Targeting 1(3):141-147 (1995)	
	48	Francisco, et al., " <i>Activity of a single-chain immunotoxin that selectively kills lymphoma and other B-lineage cells expressing the CD40 antigen</i> ", Cancer Res. 55:3099-3104 (7/15/95)	
	49	Sausville, et al., " <i>Continuous infusion of the anti-CD22 immunotoxin IgG-RFB4-SMPT-dgA in patients with B-cell lymphoma: A Phase I study</i> ", Blood 85(12):3457-3465 (6/15/95)	
	50	Mansfield, et al., " <i>Characterization of RFB4-Pseudomonas exotoxin A immunotoxins targeted to CD22 on B-cell malignancies</i> ", Bioconj. Chem. 7:557-563 (1996)	
	51	Newton, D.L., et al., " <i>Anti-tumor ribonuclease, combined with or conjugated to monoclonal antibody MRK16, overcomes multidrug resistance to vincristine in vitro and in vivo</i> ", Int'l. Oncology 8:1095-1104 (1996)	
	52	Newton, D.L., et al., " <i>Angiogenin single-chain immunofusions: influence of peptide linkers and spacers between fusion protein domains</i> ", Biochemistry 35:545-553 (1996)	
	53	Mansfield, et al., " <i>Recombinant RFB4 immunotoxins exhibit potent cytotoxic activity for CD22-bearing cells and tumors</i> ", Blood 90(5):2020-2026 (9/1/97)	
	54	Mansfield, et al., " <i>Recombinant RFB4 single-chain immunotoxin that is cytotoxic towards CD22-positive cells</i> ", Biochem. Soc. Trans. 25:709-714 (1997)	

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